BRIGHAM AND
WOMEN'S HOSPITAL

75 Francis Street
Boston, Massachusetts 02115
E-mail: adunaif@bics.bwh.harvard.edu
Tel: 617 732-8798, Fax: 617 264-5210

Andrea Dunaif, M.D.
Director, Women's Health

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Dockets Management Branch
U.S. Food and Drug Administration
Department of Health and Human Resources
Room 1061, HFA-305
5630 Fishers Lane
Rockville, Maryland 20852

Docket Number 98P-0622

To Whom It May Concern:

I am responding to the petition filed by Public Citizen Health Research Group regarding Rezulin ® (troglitazone) Tablets.

Polycystic Ovary Syndrome is considered the most common endocrinopathy affecting premenopausal women. Recent Nurses Health Study data indicates the prevalence to be approximately 7% of this population. PCOS is characterized by hyperandrogenism and chronic anovulation and is also associated with profound insulin resistance, and hyperinsulinemia. Consequently women with PCOS are considered to be at increased risk for type 2 diabetes and cardiovascular morbidity.

Insulin resistance is a unique feature of PCOS, not found in ovulatory hyperandrogenic women (1). My colleagues and I have also found that insulin-stimulated glucose utilization is decreased by 35-40% in women with PCOS, independent of obesity (2). This decrease is similar to that seen in type 2 diabetes (3). Several studies have shown prevalence rates of glucose intolerance to be as high as ~40% in obese women with PCOS (1,2,4-6). While most of these women are in their third and fourth decade of life, IGT and type 2 diabetes have also been documented in adolescents with PCOS. Thus, PCOS appears to be a major risk factor for type 2 diabetes in women, regardless of age.

Agents that decrease circulating insulin levels have been studied in women with PCOS because they may improve several of the metabolic derangements associated with the syndrome. The insulin-sensitizing agent troglitazone has been shown to improve oral glucose tolerance and insulin resistance in individuals with IGT (7,8).

My colleagues and I have documented that administration of troglitazone to women with PCOS has resulted in improved insulin sensitivity and decreased androgen excess(9). In addition, it was concluded that troglitazone improves total body insulin action, resulting in lower circulating insulin levels and that troglitazone may provide a novel therapy for PCOS.

Due to the fact that troglitazone may address both the short term symptoms as well as the long term metabolic consequences of PCOS, it is my opinion that additional research should be pursued and that the petition to ban troglitazone should be denied.

Sincerely,

Andrea Dunaif EJR

Andrea Dunaif, MD
Chief, Division of Women's Health

98P-0622

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Cc: Kathleen Reedy, RDH, MS
HHS/FDA/CDER/ORM/ACS: HFD-21
5630 Fishers Lane, Rm 1093
Rockville, MD 20857

John D. Dingell
Michigan 16th Congressional District
Washington, DC
Room 2328
Rayburn House Office Building
Washington, DC 20515
(202)225-4071

Henry A. Waxman
California 29th Congressional District
Washington DC
2204 Rayburn House Office Building
Washington, DC 20515
(202)225-3976

References:

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